Clinical Laboratory Improvement Advisory Committee

Subcommittee on Test Categorization

June 22, 1993

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Record of Attendance

The Clinical Laboratory Improvement Advisory Committee (CLIAC) Subcommittee on Test Categorization met at the Holiday Inn in Decatur, Georgia on June 22, 1993. Those in attendance are listed below:

Subcommittee Members
Dr. Paul Bachner
Ms. Michelle Best (Via Phone Link)
Dr. Stanley Inhorn
Dr. Stephen Kroger
Dr. Morton Schwartz

Ex Officio Members
Dr. Carlyn Collins, CDC
Dr. Steve Gutman, FDA
Ms. Judith Yost, HCFA (Via Phone Link)

Executive Secretary
Dr. Edward Baker

Centers for Disease Control and Prevention
Ms. Nancy Anderson
Ms. Rosemary Bakes-Martin
Mr. James Bloom
Dr. Joe Boone
Ms. Genoria Bridgeman
Ms. Carol Cook
Ms. Crystal Frazier
Dr. Edwin Holmes
Mr. Gene Matthews (CDC Legal Counsel)
Dr. John Ridderhof
Ms. Elva Smith
Ms. Julie Wasil
Ms. Rhonda Whalen
Mr. Mark White

Introduction to the Subcommittee on Test Categorization Meeting

June 22, 1993

The CLIAC Subcommittee on Test Categorization members were welcomed by Subcommittee Chairman Kroger and Executive Secretary Baker.

Subcommittee Responsibilities and the Process

Dr. Kroger briefly reviewed the purpose and scope of the subcommittee. He stated that the primary objective of the Subcommittee on Test Categorization was to review the issues of concern and make appropriate recommendations to the full committee and CDC. He expressed the desire to carry both the minority and majority views to the full committee when a consensus could not be reached. He then requested that Executive Secretary Baker serve as moderator while he participated in the discussions.

The Issues

This portion of the meeting was devoted to presentations and discussions. The topics included a legal review of the waived testing statute, an overview of FDA clearance processes, a CDC proposal for criteria of waiver, the protocol for requesting waived status, a proposed robust (high quality) test category, and a proposal for physician-performed microscopy specialty subcategories. The issues were selected by the Clinical Laboratory Improvement Advisory Committee (CLIAC) during the May 26-27, 1993 meeting.

For each issue, CDC provided a technical overview including background information and recommendations.

The public was permitted to address the subcommittee during the afternoon session. Their comments and presentation materials are incorporated into this summary as appropriate,

Review of Legal Precedence

I. Presentation

The legal interpretation was made by Mr. Gene W. Matthews, Legal Advisor to the Centers for Disease Control and Prevention and the Agency for Toxic Substances and Disease Registry.

II. Issue

What is the legal interpretation for criteria of waiver as stated in the law and regulations?

III. Subcommittee Discussion

Mr. Matthews began his discussion by stating he did not wish to complicate the issues with excessive legal interpretations. He indicted that as the law is written, the criterion for waiver is:

- *"The examinations and procedures identified in paragraph (2) are simple laboratory examinations and procedures which, as determined by the Secretary, have an insignificant risk of an erroneous result..."*

He also stated that the other listings in the regulations are simply examples. He advised the subcommittee to make their recommendations based on sound public health practices and not to fear litigation. He indicated that if a change in the law was necessary it could be addressed with Congress. The members of the subcommittee then questioned Mr. Matthews about the committee's leeway within the law. He reiterated his earlier statements. Ms. Best and Ms. Yost joined the deliberation via phone link. It was discussed and generally agreed upon that the performance characteristics of the procedure would be the most appropriate manner in which to evaluate the likelihood of erroneous results.

IV. Recommendations

Establish the criterion for waiver as:

Simple laboratory examinations and procedures which have an insignificant risk of an erroneous result.

FDA Clearance Processes

I. Presentation (See Addendum A)

The presentation was made by Steve Gutman, M.D., Medical Officer, Acting Director of Medical Devices, Division of Medical Devices, FDA.

II. Issue

What is required in the FDA processes to clear tests and test systems for home use?

III. Subcommittee Discussion

Dr. Gutman reviewed the FDA clearance procedures and noted what he believed to be limitations in the processes. He indicated that historically, quality control had not been a primary consideration in premarket product evaluation. The main criteria used by the FDA in these processes are intended use, data in support of intended use and risk of harm. He differentiated between the 510(k) and PMA processes, describing the 510(k) as more administratively streamlined, utilizing a 90 day scientific review without an external review panel. The PMA process is administratively more complex, employing a 180 day scientific review, evaluation by external scientist, and additional clinical data. Whether a test is considered 510(k) or PMA is determined by its classification status as of 1976. He suggested the processes were changing and that in some cases 510(k) submissions now require clinical data and/or panel input.

Several subcommittee members asked Dr. Gutman to clarify a few of his statements. He was asked when a product would be considered for home use. He indicated that the manufacturer must request such consideration. He was also asked how he would alter the FDA processes to accommodate the CLIA'88 regulations. He responded that he would not change these processes since the test of primary concern (the glucometer), was already on the market and he has no reservations about the other tests which have been cleared for home use. Another subcommittee member inquired if the FDA criterion for intended use could be utilized to prevent tests which were cleared for home use from being used in inappropriate settings. Dr. Gutman responded that it might be a viable alternative. He was then questioned about the appeals process for when manufacturers disagree with FDA clearance decisions. He stated that there were both informal and formal processes but that the formal legal challenges were cumbersome and seldom used. He suggested that manufacturers call FDA and express their concerns.

Criteria for Waived Tests

I. Presentation (See Addendum B)

The technical presentation was made by Ms. Rosemary Bakes-Martin, Health Scientist, Activity Chief for Quality Control and Test Categorization, Laboratory Practice Standards Branch, Division of Laboratory Systems, PHPPO, CDC.

II. Issue

What criteria should be required for consideration in the waived test category?

Ms. Bakes-Martin reviewed the following CDC proposals for criteria for waiver:

- Simple, easy to use
  - Test consist of a very limited number of steps.
  - Testing process is self-contained, requiring no operator intervention other than inserting the specimen.
  - Direct readout of results (requiring no calculation or conversion).
  - For multiple determination instruments, there is no operator intervention for specimen or analyte.
- Likelihood of erroneous results negligible
  - Performance specifications (accuracy, precision, sensitivity and specificity) do not vary more than ___ percent from the accepted reference method.
  - Fail-safe mechanism which renders no result when instrument malfunctions or result is out of reference range.

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II. Issue - CDC proposals (continued)

- No reasonable risk of harm if performed incorrectly
  - No medical action is taken solely on the results of the testother testing is required.
  - Test is performed for screening or presumptive diagnostic purposes.
- Evaluation requirements
  - Studies, such as those required by FDA, are presented to show instrument performs within designated specifications.
  - Submitted data should include precision studies performed independently at three different locations to validate day-to-day and within-day test performance and operator variability.
  - Independent field studies must be conducted to evaluate test accuracy over time in non-professional settings. The evaluations will consist of field studies using a designated number of non-professional lay persons possessing no higher than a 7th grade reading level. Without professional instruction, these people will be asked to perform the submitted tests following only manufacturer's instructions.

III. Subcommittee Discussion

Dr. Bachner expressed concern about the determination of clinical sensitivity versus analytic sensitivity. He stated that clinical sensitivity implied relevancy to a particular patient population and that this would not necessarily be appropriate to all populations for which a waived test may be used. Dr. Kroger again asked Executive Secretary Baker to serve as moderator so that he might participate more fully in the discussion. He then asked why risk of harm was still being considered as a criterion and why specimen collection was not addressed. Dr. Collins indicated that CDC was concerned with specimen acquisition but that the proper language had not yet been defined. She proposed the inclusion of a statement suggested by CAP that there be "no preanalytical sources of error". Dr. Schwartz stated that he believed that the proposed requirement "No *medical action is taken solely on the results of the test*," was unrealistic.

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III. Subcommittee Discussion (continued)

Dr. Kroger concurred. Ms. Best also agreed and stated that she would like to see the language *"Screening, presumptive diagnosis and disease monitoring purposes"* included under the CDC proposed criterion *"likelihood of erroneous results negligible."* Dr. Bachner agreed and asked if CDC would consider rewording this criterion. Dr. Kroger voiced concern about utilizing that language as he didn't believe the committee should be defining an intended use for waived testing. Dr. Bachner and Dr. Inborn agreed and further suggested that the entire *"risk of harm"* criterion be stricken from the CDC proposals. Dr. Schwartz then commented that he would like the direct readout statement under the CDC proposed "Simple and *easy to use"* criterion clarified for instruments without readouts. He stated that under the proposed criterion *"likelihood of erroneous results negligible,"* the performance specifications would need to be analyte dependent and very specific. He asked that the second bullet under this criterion be revised to read "Fail-safe mechanism which renders no result when instrument malfunctions or result is out of linear range." He also recommended that the proposed *"no medical action is taken solely on the results of the test"* requirement be revised to possibly read *"Must reproduce results prior to taking medical action.* " Several subcommittee members voiced their agreement. A general discussion of waived testing followed. Ms. Yost questioned whether system stability was being considered in the CDC proposals. Ms. Best stated she would be uncomfortable with any process where the committee would be required to review and move tests to the waived category. Some subcommittee members suggested using the requirements for following "good laboratory practice" and "all manufacturer's instructions" to improve laboratory testing by requiring the manufacturers to include the appropriate quality control instructions. One subcommittee member proposed removing the glucometers from the waived test listing and placing them in a regulated category. Another suggested revising the FDA "intended use" criterion to help define where a test or test system may be used. The subcommittee suggested that CDC evaluate the tests and devices currently in the waived category against its proposed criteria.

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IV. Recommendations

The subcommittee recommended that CDC revise its proposed criteria as follows:

- *Simple and easy to use:*
  - Revise the statement concerning direct readouts to address non-instrument tests.
- *Likelihood of erroneous results negligible:*
  - Correct the second bullet under this criterion to read:

    "Fail-safe mechanism which renders no result when instrument malfunctions or result is out of linear range."
  - Add a statement to address the stability of the device.
  - Add a statement which evaluates preanalytic considerations, particularly specimen collection.
  - Add a statement that performance specifications will be analyte dependent.
- *No reasonable risk of harm if performed incorrectly:*
  - Eliminate this criterion entirely.
- *Evaluation requirements:*
  - No formal recommendations were made concerning this criterion.

Protocol for Requesting Waived Status

I. Presentation (See Addendum C)

The presentation was made by Ms. Elva Smith, Health Scientist, Quality Control and Test Categorization Activity, Laboratory Practice Standards Branch, Division of Laboratory Systems, PHPPO, CDC.

II. Issue

What is the process for requesting waived status for tests and test systems?

Ms. Smith reviewed the process for requesting test system or assay evaluation for waived test status. The FDA and CDC will concurrently evaluate all requests for waiver. Recommendations for waiver will be presented to CLIAC for input prior to making a final determination.

III. Subcommittee Discussion

The subcommittee thanked CDC for this clarification.

Robust (High Quality) Test Category

I. Presentation (See Addendum D)

The technical presentation was made by Carlyn Collins, M.D., M.P.H., Director, Division of Laboratory Systems, PHPPO, CDC.

II. Issue

Is a robust (high quality) test category needed?

Dr. Collins examined the potential for adding an additional test category, robust testing, which would be high quality, low complexity testing with built in quality control. This category would require proficiency testing (PT) and would be performed only in a clinical setting. Inspection would be required in the case of failed or poor proficiency testing.

III. Subcommittee Discussion

Dr. Kroger yielded the chair to Dr. Baker in order to participate in the discussion. Dr. Collins was asked how these test could be restricted to clinical settings. She responded that this could be accomplished through personnel standards. Ms. Best inquired as to whether a laboratory director would be required. Dr. Collins responded that a laboratory director would be required. Dr. Bachner indicated that his initial response to this proposal was favorable and agreed that the development of the appropriate personnel standards would be crucial. Dr. Kroger, Dr. Schwartz and Ms. Best also voiced support, but preferred that the category remain limited. Dr. Gutman advised that the personnel standards be technology based and that this might serve to encourage manufacturers to increase the number and types of these test systems available. Dr. Collins clarified the CDC proposal, indicating that the requirements for quality assurance (QA), quality control (QC), proficiency testing (PT), and patient test management would be the same as for moderately complex laboratories. Inspections would not be required unless there were proficiency testing problems. Dr. Bachner suggested that a director be required and that he be totally responsible for the quality of testing, but that sequential proficiency testing failure should trigger an inspection. Dr. Gutman remarked that some type of randomized inspection is necessary to keep quality high. Dr. Kroger, Dr. Schwartz, Ms. Best and Ms. Yost agreed. Dr. Schwartz suggested that CDC apply the proposed requirements to the tests most frequently performed in physicians' office laboratories (POL) and report back to the committee.

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III. Subcommittee Discussion (continued)

Dr. Bachner and Dr. Kroger supported this suggestion. Dr. Inhorn pointed out that this category may not be helpful to public health testing and questioned for whom the category was intended. Several subcommittee members observed that adding such a category with its built in QA, QC and PT would not relieve the POL's regulatory burden, Dr. Baker summarized the deliberations as follows:

- There is a need to identify whether or not this category is potentially useful.
- The personnel requirements would be critical.
- A laboratory director would be required.
- Inspection should be random as well as triggered by failed proficiency testing or complaints.

IV. Recommendations

The subcommittee asked CDC to apply the proposed requirements to the tests most frequently performed in POL's and report back to the committee.

Physician-Performed Microscopy Specialty Subcategories

I. Presentation (See Addendum E)

The technical presentation was made by Ms. Nancy Anderson, Quality Control and Test Categorization Activity, Laboratory Practice Standards Branch, Division of Laboratory Systems, PHPPO, CDC.

II. Issue

Should specialty subcategories be added to the physician-performed microscopy category?

Ms. Anderson reviewed the CDC's proposed criteria for PPM specialty subcategories.

III. Subcommittee Discussion

Dr. Bachner asked if the intent was to extend these to mid-level practitioners. The response was that only board certified physicians were currently under consideration. He suggested that the wording be changed to *"the exam is an integral part of patient management during the patient visit."* He also indicated that he believed that "board certified" and "adequate training" were not practical concepts. Dr. Kroger stated that while the subcommittee believed these individuals must be properly qualified, they were not sure how to determine the adequacy of training. Dr. Inhorn indicated did not believe that the experience received in most programs constituted clinical laboratory experience. Ms. Best indicated that she would not be in favor of including less formal training. Dr. Baker summarized the subcommittee's discussion and requested that CDC prepare one or two specialty subcategories for presentation to CLIAC. Dr. Kroger stated that he believed formation of these subcategories may exceed the authority of CLIA. He suggested that the best solution would be to require a letter from the physician's training program indicating the physician was trained to perform these tests. Dr. Collins requested clarification of the subcommittee's recommendations. Dr. Bachner suggested that an outline be made of what would be considered as appropriate training and that he would be in favor of a fairly liberal interpretation. He added that his concern was primarily one of limiting access to patient care and not one of tests occasionally being performed incorrectly. Dr. Collins requester] clarification as to whether mid-level practitioners would be included. The subcommittee was divided and ambiguous in its response.

IV. Recommendation

The subcommittee recommended that CDC prepare one or two specialty subcategories for presentation to CLIAC.

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Public Comments

(See Addendum F)

Dr. Sheldon Schaffer, Vice President of Regulatory Affairs and Business Development for Cholestech, made a public comment. He expressed frustration with the committee's decision to move some tests into the waived test category despite the moratorium. He indicated that the manufacturers would like a "level playing field" and immediate consideration of those lipid test systems similar to the one which was moved to the waived category.